## REMARKS

Claims 1-11 are pending. Claims 5-7 and 9-11 are withdrawn from consideration. Claims 1-4 have been amended. Therefore, claims 1-4, and 8 are pending in the application.

Support for these amendments appears throughout the specification and claims as originally filed including at page 6, lines 20-21; page 8, line 22 through page 9, line 12; and in claim 4 as originally filed. No new matter is introduced by these amendments. Applicants make such amendments without prejudice to pursuing the originally presented or cancelled subject matter in a later application claiming benefit of this application, and particularly without prejudice to determination of equivalents of subject matter of this application or any later application claiming benefit of this application.

### Specification/Claim Objections

Applicants have amended the specification to include the terms "chronic obstructive pulmonary disease", "nonsteroidal anti-inflammatory drugs", "dimethylsulfoxide", and "[4-(2-hydroxyethyl)-1-piperazineethanesulfonic acid]" to define the acronyms "COPD", "NSAIDS", "DMSO", and "HEPES" respectively for their first instance of use. Applicants point out that the acronym "HBSS", as used in the specification, stands for "Hank's balanced salt solution", and is spelled out in its first instance of use at page 24, line 24 in the specification.

Applicants have also amended the specification to correct the spelling of "sarcosine" and to subscript the numerical characters in the chemical formulae that define the variable "Y" (e.g., "$COOCH_3$").

### Rejections under 35 U.S.C. 112, Second Paragraph

Claims 1-4 and 8 are rejected as being indefinite. It is alleged that "Claim 1 is unclear as to whether or not 'a pharmaceutically acceptable salt' refers to 'U' or to the 'cyclosporin' (Action, page 3, lines 5-6). Applicants have amended claim 1 to clarify that the pharmaceutically acceptable salt refers to the cyclosporin. To make this distinction, Applicants have replaced the comma between the end of the definition of "U" and the beginning of the

phrase "or a pharmaceutically acceptable salt" with a semicolon (see claim 1 as originally filed, page 26, line 25). Support for this amendment can be found in the specification including at page 6, lines 20-21. Applicants therefore respectfully request that this rejection be withdrawn from claim 1 and from claims 2-4, which depend from claim 1.

Claim 2 is rejected as being indefinite for "lack of a period at the end of the claim recitation" (Action, page 3, line 7). Applicants submit that the rejection no longer applies to claim 2 as amended.

Claim 4 is rejected as being indefinite for "lack of punctuation ';' or ',' between members of the Markush group and the absence of an 'and' or an 'or' between the second to last and the last recited member of the Markush group" (Action, page 3, lines 8-10). Applicants submit that the rejection no longer applies to claim 4 as amended.

Rejections under 35 U.S.C. 102(b)

Claims 1-4 and 8 are rejected as being anticipated by Wang, N.Y. *et al.*, U.S. Patent No.: 5,239,037 (Wang). It is stated in the Action that:

> Wang et al. disclose a cyclosporin structure that meets the limitations of the Formula (I) structure of claim 1 of the instant application (see patent column 8, formula III wherein "W" is 1 carbon atom, "Y" is Oxygen atom, "m" = 0, and "Z" is $OR_a$ [$R_a$ = -$CH_3$]). Since Applicant elects "B" as –α-amino butyric acid, "U" as –(D)-alanine, "X" as absent, and "Y" as $COOCH_3$ for patent examination, claims 2-4 are anticipated by the patent reference as well.

The compound in Wang cited in the Action: is compound **11** (Wang reference number), [7-methoxycarbonyl-3-(R)-hydroxy-4(R)-methyl-2-(S)-methylamino-6-heptenoyl]$^1$cyclosporin A.

Applicants have amended independent claim 1 with respect to the definition of the C(O)-O-$R^1$ group in the definition of the "Y" group. Specifically, the definition of $R^1$ has been amended to recite a "C1-C6 alkyl substituted with halogen, heterocyclic, aryl, C1-C6-alkoxy, C1-C6 alkylthio, halogen-substituted C1-C6 alkoxy, or halogen-substituted C1-C6 alkylthio." Thus, $R^1$ is defined to be particular substituted alkyl groups. Hydrogen and unsubstituted "C1-C6 alkyl", i.e., saturated straight- or branched-chain hydrocarbon radicals containing between

one and six carbon atoms (see Specification, page 12, lines 7-9) are not recited in the amended definition of $R^1$.

The term $R^1$ in claim 1 corresponds to the term $R_a$ of Formula (III) in Wang. In the compound cited by the Examiner, i.e., compound **11**, $R_a$ is a methyl group ($-CH_3$), which is an alkyl group that falls within the definition of unsubstituted "C1-C6 alkyl." Compound **11** does not read upon claim 1, as amended, because it contains an unsubstituted alkyl ester group. This contrasts with the compounds covered by claim 1, which have Y groups having $R^1$ groups that are substituted alkyl ester groups. Thus, claim 1 is not anticipated by Wang. Since claim 2 depends from claim 1, claim 2 is also not anticipated by Wang. Finally, dependent claims 3 and 4 have been amended to comport with the scope of $R^1$ in amended claim 1. Applicants therefore submit that claims 1-4 are not anticipated by Wang and request withdrawal of this rejection.

Claim 8 is also rejected as being anticipated by Wang. It is alleged in the Action that:

> Wang et al. teach a carrier that is a poly(amino acid) or bovine serum albumin (see column 4, lines 24-29), as applied to claim 8 of the current application (Office Action, page 4, lines 4-5).

Applicants disagree. The uses of the term "carrier" in Wang and in Applicants' claim 8 are distinguishable and different. The pharmaceutical composition of claim 8 comprises "a cyclosporin compound of claim 1 together with a pharmaceutically acceptable diluent or carrier therefor." The specification clearly defines the term "pharmaceutically acceptable carrier" to mean "a non-toxic, inert solid, semi-solid or liquid filler, diluent, encapsulating material or formulation auxiliary of any type" (Specification, page 15, line 23 through page 16, line 1). Thus, the composition contains a cyclosporin compound and a distinct and separate, e.g., filler, substance.

Wang *et al.* teach a carrier that is a poly(amino acid) or bovine serum albumin. However, the term "carrier" as used in Wang refers to a carrier molecule that is covalently linked to a cyclosporin-based hapten:

> The present invention also relates to novel cyclosporin A compounds substituted at and conjugated to an antigenicity-conferring carrier through a

derivative formed at the first amino acid residue...The preferred carrier is a poly(amino acid), most preferably bovine serum albumin (BSA) (Wang at column 4, lines 21-24; lines 27-29).

Thus in the case of cyclosporin A derivatives bearing a reactive functional group this will be any group capable of reaction with a carrier molecule, e.g., a protein molecule, to provide a co-valently linked conjugate with said carrier molecule...(Wang column 6, lines 61-65).

[H]aptens are precursors of the immunogens, comprised generally of cyclosporin A...The immunogens of the present invention are made by coupling a hapten, such as that shown in Formula (II), to a poly(amino acid) (Wang at column 9, lines 1-3 and column 10, lines 1-4).

Clearly the meaning of the term "carrier" in Wang is distinct and different from the meaning of the term in Applicants' claim 8. In Wang, "carrier" refers to an antigenicity-conferring molecule that is covalently linked to a cyclosporin. On the other hand, the term "carrier" as used in Applicants' claim 8 refers to a non-covalently linked, inert substance that serves the role of a non-toxic filler, diluent, etc. for a cyclosporin-containing pharmaceutical composition. Applicants' cyclosporin structure is not covalently linked to the "carrier" in their composition, while Wang's compounds are, in fact, cyclosporin derivatives (i.e., polyaminoacid or BSA conjugates). Thus, Applicants submit that Wang does not anticipate claim 8. Applicants therefore respectfully request that the rejection be withdrawn.

Provisional Rejections-Obviousness Type Double Patenting

Claims 1-4 and 8 are provisionally rejected under the judicially created doctrine of double patenting over claims 1-4 and 11 of copending Application No. 09/976219 and claims 1-4 and 9 of Application No. 09/975923 (Action page 5 line 7 through page 7, line 9).

Applicants disagree with the assertions in the Action regarding obvious structural variation. Applicants will address these issues upon maturation of any of the instant or cited applications into a granted patent.